At the time of transplant, 21 pts (57%) were in complete remission (CR) (CR1 = 20%) and 16 had relapsed/refractory disease. Grafts consisted of double (29 pts) or single (8 pts) CB units. Donor recipient HLA matching (n = 66 units) was 3/6 (n = 1, 1.5%), 4/6 (n = 47, 71.2%) and 5/6 (n = 18, 27.3%) alleles. Median TNC infused was $1.8 \times 10^7$/kg (range 1–5.8). 19 pts received ex-vivo expanded units. The conditioning regimen consisted of melphalan 140 mg/m$^2$ on day -8, thiotepa 10 mg/m$^2$ on day -7, fludarabine 160 mg/m$^2$ over 4 days on days -6 to -3, and rabbit ATG 1.25 mg/kg on day -4 and 1.75 mg/kg on day -3 (FMT). Patients with CD 20+ lymphoid malignancies also received rituximab 375mg/m$^2$ on day -9 (n = 8, 22%). GVHD prophylaxis was tacrolimus and mini-methotrexate in 23 (62%) and tacrolimus and mycophenolate in 14 pts (38%).

**Results:** 34/36 evaluable pts (95%) engrafted neutrophils and had hematopoietic recovery with 100% cord blood-derived cells. At day 30, of the 29 pts who received a double CBT, 75% had chimerism derived entirely from one donor while 25% had mixed donors chimerism. Neutrophil recovery occurred after a median of 21 days (range 6–45) and platelet recovery after a median of 37 days (range 26–134, N = 24; 67%). 32/37 pts (87%) were in CR after transplant with 16 surviving after a median follow-up of 12.1 months. Thirteen pts (36%) developed gr II-IV aGVHD (gr III-IV aGVHD in 5 pts, 14%), and 13 of 32 pts had cGVHD (40%), with the majority experiencing extensive GVHD. 11 pts (29.7%) relapsed after a median of 7 months post transplant and 12 died of non-relapse causes. Day-100 treatment-related mortality (TRM) in this heavily pre-treated population was 10%. Overall, causes of death included disease relapse (n = 9), infections (n = 6), organ failure (n = 3), pulmonary hemorrhage (n = 1) and GVHD (n = 2).

**Conclusions:** The FMT regimen is associated with a high rate of engraftment and low TRM in adult pts undergoing CBT which supports its further evaluation in CBT.

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### ALTENATIVE DONOR PERIPHERAL STEM CELL TRANSPLANT (PSCT) WITH CD3+ DEPLETION AND CD3+ ADDBACK FOR PEDIATRIC PATIENTS WITH LEUKEMIAS

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Most patients (pts) with leukemias who may benefit from allogeneic HSCT lack matched related donors (MRD), and due to diverse ethnic backgrounds, matched unrelated donors may be unavailable in a timely fashion. High doses of mobilized PSCs may decrease time to engraftment and relapse risk, but most studies report an increased risk of extensive chronic GVHD. Partial T depletion allows the use of alternative donors, while potentially retaining graft vs leukemia(GVL) effect and ensuring engraftment. We began a pilot study in 2005 for pts with leukemias or myelodysplastic syndromes who lacked MRD using CD3+ depleted PSCs with a defined dose of CD3+ at the time of infusion. Conditioning included thiotepa 5mg/kg × 2 d, cyclophosphamide 60 mg/kg × 2 d, TBI 1200 cGy. Clinimacs device was used for CD3+ depletion, and an aliquot of intact PSCs was cryopreserved for potential donor lymphocyte infusion (DLI). GVHD prophylaxis included cyclosporine followed by oral tacrolimus. Initial CD3+ dose was $0.2 \times 10^5$/kg, but this was escalated to a maximum of $5 \times 10^5$/kg depending upon HLA disparity. This report includes the first 28 pts with at least 6 months follow up (median, 18 months, 9–41). Patients included 17 males, median age 12 years (0.8–20). Diagnoses included ALL -13, AML - 6, MDS/MPD-5, JMML-1,CML-3. Donors were unrelated for 25, and related (father, brother, aunt) for 3. Donors were high resolution 10/10 matched for 8 pts (30%); 7 had single antigen or allele mismatches, 9 had 2 mismatches and 4 had 3. Pts received a median of $5 \times 10^6$/kg CD34+ (3–10) and a median of $1.8 \times 10^5$/kg CD3+ (0.5–8). Engraftment occurred in all pts, with ANC>500 at a median of 16 days (10–26) and platelets >20k at a median of 13 days (8–28). Acute GVHD occurred in 17 pts, and was overall grade I-II in 14, III-IV in 3 (10.7%) Chronic GVHD developed in 7/24 evaluable pts (29%) and was extensive in 4 (17%). TRM occurred in 5 pts before d+175 from ARDS (1), liver failure/VOD (2), invasive fungus (1) and GVHD/MSOF (1). Relapses occurred in 5 pts (ALL-3, AML/MPD-2) at 3- 12 months and 2 CML pts developed mixed chimerism. Three pts with AML, MPD, and CML who received DLI have full donor chimerism 24–41 months post SCT. EFS is 57% and OS 68 % including pts in remission following DLI. CD3+ depletion with a defined dose of CD3+ provides durable engraftment, maintains GVL, and allows use of mismatched donors. Additional study is needed to define optimal dose and type of T cell addback.

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### THE IMPORTANCE OF BLOOD CYCLOSPORINE LEVEL DURING FOUR WEEKS AFTER UNRELATED CORD BLOOD TRANSPLANTATION TO PREVENT SEVERE GRAFT-VERSUS-HOST DISEASE

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We studied the clinical outcomes of 113 adults with hematologic malignancies who received unrelated cord blood transplantation (CBT) after myeloablative preparative regimens including 12 Gy total body irradiation. All patients received same graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporine (CsA; 3mg/kg intravenous infusion over 10 hours) and short-term methotrexate (MTX; 15mg/m$^2$ on day1 and 10mg/m$^2$ on days 3 and 6). CsA was reduced due to impaired renal function or was tapered beginning between weeks 6 and 9 in the absence of GVHD in our protocol. Median number of nucleated cells in infused cord blood was $2.37 \times 10^7$/kg (range 1.73 to $5.29 \times 10^7$/kg). Cord blood grafts were mismatched 0 to 4 of 6 HLA-A, -B (antigen level), and -DRB1 (allele level) to the recipient. Engraftment was achieved in 105 of 113 patients and those were subjected to be analyzed for acute GVHD. Of the 105 evaluable patients, the incidence of grade II to IV and III to IV acute GVHD was 62.9 % and 8.6 %, respectively. Ninety five patients survived more than 100 days and extensive type chronic GVHD occurred in 24.2 %. Of the 113 patients, 72 were alive and disease-free between 333 and 3658 days after CBT (median 1558 days). In 105 evaluable patients, median day of tapering and 50% reduction of CsA was 28 (range 0 to 110) days and 39 days (range 4 to 142) after transplantation, respectively. The average of trough CsA level after 1 week, 2 weeks, 3 weeks, and 4 weeks was 177, 149, 160, and 166 ng/ml, respectively. In 54 of 105 patients, trough CsA levels were more than 160 ng/ml on day 28 and none had grade III to IV acute GVHD. The incidence of extensive type chronic GVHD was 13.7 % in 51 evaluable patients whose trough CsA levels were more than 160ng/ml on day 28. These results suggested that cyclosporine and short-term MTX effectively prevented the occurrence of severe GVHD after myeloablative CBT and blood CsA levels should be monitored carefully during early phase after transplantation.

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### ANTIBODIES ARE DETECTED AGAINST MISMATCHED HLA CLASS II ALLELES AND NOT CLASS I FOLLOWING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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This pilot study sought to determine whether alloantibody to HLA is made in patients with acute GVHD. Day 100 serum samples of 40 recipient-donor pairs of (theoretically) single antigen/allele HLA-mismatched (MM) unrelated donor transplants performed between July 1990 and June 1999 were obtained in collaboration with the CIBMTR and NMDP. All recipients had developed acute GVHD. We measured HLA class I and II antibody (Ab) levels to the MM alleles in both the graft-versus-host (GVH) and host-versus-graft (HVG) directions. Allele level typing for eight loci (A, B, C, DRB1, DQB1, DQA1, DPB1, DPA1) was compared between donor and recipient to identify all mismatches. GVH disparity meant the allele expressed in the recipient was absent in the donor. HVG disparity meant the allele expressed in the donor was absent in the recipient. In general, we observed more than a single allele MM in these pairs. Sera were screened for IgG antibody to the MM HLA alleles using single antigen beads covering 96 different class I